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### Electronic Clinical Decision Support System for allergic rhinitis management

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## Electronic Clinical Decision Support System for allergic rhinitis management

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Running title: Development of *Allergy Diary Companion* app

## Summary

Background: Allergic rhinitis (AR) management has changed in recent years following the switch from the concept of disease severity to the concept of disease control, publication of the AR clinical decision support system (CDSS) and development of mobile-health (m-health) tools for patients (e.g. *Allergy Diary*). The *Allergy Diary Companion* app for health care providers is currently being developed and will be launched in 2018. It incorporates the AR CDSS to provide evidence based treatment recommendations, linking all key stakeholders in AR management.

Objective: To produce an electronic version of the AR CDSS (e-CDSS) for incorporation into the *Allergy Diary Companion*, to describe the app interfaces used to collect information necessary to inform the e-CDSS and to summarize some key features of the *Allergy Diary companion*.

Methods: The steps involved in producing the e-CDSS and Incorporating it into the *Allergy Diary Companion* were (i) generation of treatment management scenarios; (ii) expert consensus on treatment recommendations; (iii) generation of electronic decisional algorithms to describe all AR CDSS scenarios; (iv) digitization of these algorithms to form the e-CDSS; and (v) embedding the e-CDSS into the app to permit easy user e-CDSS interfacing.

Results: Key experts in the AR field agreed on the AR CDSS approach to AR management, and on specific treatment recommendations provided by *Allergy Diary Companion*. Based on this consensus, decision processes were developed and programmed into the *Allergy Diary Companion* using Titanium Appcelerator (Javascript) for IOS tablets. To our knowledge this is the first time the development of any m-health tool has been described in this transparent and detailed way, providing confidence, not only in the app, but also in the provided management recommendations.

Conclusion: The *Allergy Diary Companion* for providers, provides guideline and expert-endorsed AR management recommendations. [MASK paper N° 32]

## Introduction

The aim of allergic rhinitis (AR) management is to achieve control of the disease and its symptoms [1, 2], and is a dynamic process. Control can fluctuate over time influenced by many factors, including AR phenotype (i.e. intermittent or persistent AR), environmental exposure and current treatment. Therefore, the tool used to measure disease control must be simple, suitable for everyday use and sensitive to change. A simple visual analogue scale (VAS) has been recommended as the language for assessing AR control [2-4]. It has recently been converted to electronic format and included in a free mobile app for patients - *Allergy Diary* – as part of MASK (Mobile Airways Sentinel network) [5-8].

The *Allergy Diary* aims to empower patients to self-manage their AR [5, 6]. The use of self-management and information & communication technology may hold the key to chronic disease management, and provides useful objective data for physicians.

The VAS has also been Incorporated into an AR clinical decision support system (CDSS), a new type of disease management tool [2]. A CDSS is a health information technology system, based on the best evidence and algorithms, designed to provide physicians, and other health care providers, with clinical decision support (i.e. assistance with clinical decision-making tasks). It is an important tool

for precision medicine [9, 10]. Within the AR CDSS, the VAS is used to assess AR control and to assist in making management decisions, assisting patients and health care providers to jointly determine AR treatment and its step-up or step-down strategy depending on the status of AR control [2].

The next step is to integrate the AR CDSS into an app for providers called *Allergy Diary Companion*, by producing an electronic version of it (e-CDSS). The *Allergy Diary Companion* app is designed for use during a patient-physician consultation. The e-CDSS will effectively be the 'brain' of the app, providing guideline-directed AR management recommendations in response to 4 inputs: VAS score, Allergic Rhinitis & its Impact on Asthma (ARIA)-defined AR phenotype, allergen exposure and AR treatment history. This article describes the production of the e-CDSS from the paper version [2] for incorporation into the *Allergy Diary Companion*. Expert consensus on AR-CDSS recommendations, as well as the production of decision process to describe this consensus and programme the app are also described. Finally, description of the various interfaces used by the app to collect information necessary to inform the e-CDSS and key features of *Allergy Diary Companion* are summarized.

## Methods

From the AR CDSS to the e-CDSS

Figure 1 outlines the six steps involved in the transformation of the paper AR-CDSS to the e-CDSS (Suppl. Figure 1A & B) [2].

*AR treatment scenario identification*

### **Step 1: Major scenarios on AR management approach**

Thirteen major scenarios were identified from the AR CDSS (S-Table 1). These scenarios incorporated VAS score cut-offs, ARIA-defined AR phenotype (i.e. intermittent or persistent AR) and AR treatment,

and provided an AR management approach (i.e. when to initiate treatment, continue, step-up and step-down treatment). T0 represents no treatment. For the purpose of these scenarios, AR treatments were coded as:

- T1: Non-sedating H<sub>1</sub>-antihistamines (oral, intranasal, intraocular), leukotriene receptor antagonists (LTRA), cromones (intranasal or intraocular)
- T2: Intranasal corticosteroid (INCS)
- T3: INCS + azelastine (AZE)
- T4: Oral corticosteroids (as add on to local treatment)
- T5: Consider referral to an allergist and allergen immunotherapy (AIT)

The AR CDSS is an algorithm for the acute symptomatic treatment of AR. Recommendations on the benefits and use of AIT may be found elsewhere [11].

## **Step 2: Specific AR treatment recommendations**

From these 13 major scenarios, 34 detailed scenarios were [2]. Inputs considered included disease phenotype (i.e. intermittent/persistent), allergen exposure, VAS score and current treatment and specific AR management recommendations were provided (S-Tables 2, 3, 4 & 5).

### *Key opinion leader consensus on AR CDSS treatment recommendations*

## **Step 3: Survey of experts**

These 34 detailed scenarios were incorporated into a survey that was delivered by an online service, Survey Monkey ([www.surveymonkey.com](http://www.surveymonkey.com)), and sent to 70 experts on AR and ARIA members from 23 countries, in order to achieve consensus and improve robustness of the AR CDSS algorithm. Experts were selected for their expertise (i.e. general practice, allergy, ENT, respiratory medicine, pharmacy, public health) with a global representation. We aimed at a 50% response rate. The survey was divided into 4 parts: (i) general approach to AR treatment (i.e. when to initiate, continue, step up or step down treatment; n= 8 questions; S-Table 2); (ii) treatment step up (i.e. what treatment to

step up to considering current treatment; n= 11 questions; S-Table 3); (iii) treatment step down (i.e. what treatment to step down to considering current treatment; n = 12 questions; S-Table 4); and (iv) treatment initiation (i.e. what treatment to start with, considering VAS score and AR phenotype; n= 3 questions; S-Table 5). Experts indicated their level of agreement for each of the 34 presented scenarios on a VAS ranging from 0 mm (strongly disagree) to 100 mm (strongly agree). A response was returned by 35 experts (response rate: 50%) from the USA and Canada (n=5), Europe (n=26), South America (n=2) and Australia (n=2).

Individual scores for each of the 34 scenarios were tabulated, averaged and categorized in the classical way: survey VAS score 0-25 mm (poor agreement); 25-49 mm (fair agreement); 50-74 mm (good agreement); 75-100 mm (excellent agreement) (S-Figure 2A). Excellent expert consensus was achieved for all step up scenarios except scenarios 11 (survey VAS score: 64 mm, 13 (survey VAS score: 64 mm), and 14 (survey VAS score: 64 mm) which all dealt with step up from T3 (S-Table 3; S-Figure 2A). Excellent expert consensus was also achieved for all step down scenarios except scenarios 20 (survey VAS score: 74 mm) and 21 (survey VAS score: 66 mm) which dealt with step down from T3 or T2, respectively (S-Table 4; S-Figure 2A). The reasons for these lower consensus scores and resolution of these issues is provided in the online supplement.

#### **Step 4: Scenario modification and summary of findings**

An email was sent to all experts who provided a survey VAS score <50 mm for any scenario to (i) understand the reason for disagreement and (ii) achieve consensus on a resolution. Experts were permitted to change their original survey VAS scores based on the results of this discussion process (these changes are shown in red font in S-Figure 2B). Expert agreement increased to a VAS score >75 for all scenarios that were considered a second time. Details of expert comments on the scenarios, and the response and resolution are provided in the online supplement.



### Step 5: Digital specifications of AR CDSS (all scenarios and modifications)

The next step was to digitally specify the agreed scenarios to generate a series of digital rules used to programme the *Allergy Diary Companion* (Ecole des Mines, Ales). The first task was to define a set of representative scenarios with experts of the domain, taking into account all possible parameters (e.g. VAS, ongoing treatment, type of patient). Then, scenarios were translated into a graphical representation, providing an algorithm, which allowed the recommendations to be automatically defined (Figure 2 A-D). The algorithm was validated in several ways: (i) review with experts, (ii) review of recommendations and (iii) transformation of the algorithm into a *state machine* (i.e. a model representing the *state cycle* of a patient.) The process enabled verification that the patient *state* may evolve, depending on adequate value of VAS, and according to all possible treatment transitions (i.e. from “no treatment” to “under treatment”, staying “under treatment” and come back to “no treatment”). These verifications ensured that all possible situations were taken into account in a systematic way.

**Step 6:** Finally, a total of 77 scenarios (all possible scenarios) were programmed into the *Allergy Diary Companion*. The app was programmed and designed by Peercode, Netherlands, using the digital specifications above (including expert treatment recommendations), ensuring consideration of each possible input into the app. It was developed in titanium appcelerator (Javascript) for tablets on the IOS platform, and is easily translated and modified. Usability of the app and reliability of the treatment recommendations it provides has been checked by Peercode and further validation is currently ongoing prior to launch. The app requires no internet function after download.

## Results

### Summary of survey results

Mean scores for each question were calculated to show the level of consensus for each of the 34 AR CDSS scenarios (Table 1 and S-Figure 3 A-D). Experts endorsed the AR CDSS approach, with good agreement achieved on step-up and step-down treatment recommendations. In summary:

- AR treatment should be stepped up for treated AR patients with a VAS score  $\geq 5/10$  cm.
- For patients with VAS score  $\geq 2$  to  $<5/10$  cm, treatment should be continued for patients with intermittent AR (IAR) and continued or stepped up for those with persistent AR (PER).
- Treatment should be stepped down for patients with a VAS score  $<2/10$  cm.
- When step up treatment is recommended, patients on T1 should be stepped up to T2 OR T3
- When step up treatment is recommended, patients on T2 should be stepped up to T3.
- Short course oral corticosteroids (i.e. T4) may be added here if necessary.
- Patients should be referred (e.g. to ENT or allergy specialists) if VAS score remains  $\geq 5/10$  cm or if there is a need for oral corticosteroids.
- When step up treatment is recommended, patients on multiple therapies should be stepped up to T3, and T4 added on (short course to minimise side effects and only if necessary)
- Stepping down treatment was essentially the same in reverse, with the proviso that patients with nasal congestion should be stepped down to an INCS-containing regimen in preference to T1 (albeit many patients will self-medicate and stop treatment).\*\*
- Treatment step-up and step-down strategies remain the same irrespective of AIT status.\*

\*: Does not consider the indication of AIT

\*\*: Modified after expert consensus

## Digital specification of the e-CDSS modules

In order to make a treatment recommendation, the CDSS within the *Allergy Diary Companion* must be 'fed' with information. We have described this information as modules (Table 2) with each of modules 1, 2 and 3 providing the input necessary for module 4 (i.e. e-CDSS)

**Module 1 (VAS score):** During physician consultation or pharmacist visit, patients generate a VAS score using their finger and the touch screen functionality of an iPad, allowing selection of VAS score from 0 to 10 cm (inclusive). For the purpose of the e-CDSS, VAS scores are categorized as  $\geq 5/10$  cm (uncontrolled AR),  $\geq 2$  to  $< 5/10$  cm (partly-controlled AR) and  $< 2/10$  cm (well-controlled AR) (Table 2), the same as those cut-offs used by *Allergy Diary*. These cut-offs were selected based on clinical studies in both asthma and rhinitis [12-17].

**Module 2 (treatment classification system):** The purpose of this module is to define the class(es) of current AR medications used by patients. A simple alpha-numeric system was used for the e-CDSS, with treatments classified from T0 (no treatment) up to T5 (consider referral and AIT) (Table 2).

**Module 3 (patient information):** Patients input this information into the *Allergy Diary Companion* during physician consultation. The information gathered (or computed) includes:

- Specific AR medication currently used
- AR phenotype (i.e. IAR or PER)
  - AR phenotype is classified according to duration of medication use (Questions 3a and 4a, Table 2) or duration of symptoms for untreated patients (Questions 3b and 4b, Table 2)
- Allergen exposure status
  - Information on what constitutes an allergen is provided for patients

AR medication(s) are selected from a scrolled list of all over the counter or prescribed medications available in each country (Question 2a, Table 2). Multiple medication selections are permitted. For each medication class selected, a corresponding treatment code is assigned by the system. Exposure

to allergen is assessed using a simple true or false algorithm (Table 2). S-Figure 4 shows the organogram of the sequence of questions that patients answer in Module 3. At any step, the patient can go back to a previous question to correct his/her answer, or cancel the survey answer. No personal information is collected.

**Module 4 (e-CDSS specifications):** The e-CDSS uses data obtained from the other modules to deliver a recommendation corresponding to the most appropriate treatment. Table 2 summarizes how this information is gathered, the input used by the e-CDSS to make a decision and the variables used (online supplement). Information from each of these modules is used to produce treatment recommendations. The decision processes underlying treatment recommendations are shown in Figure 2 (A-D). Four decision processes were developed to cover 4 scenarios: (i) the patient is not currently on any AR medication (Figure 2A), (ii) the patient has well-controlled AR (i.e. VAS score <2 cm; Figure 2B), (iii) the patient has partly-controlled AR (i.e. VAS score  $\geq 2$  to <5 cm; Figure 2C), (iv) the patient has uncontrolled AR (i.e. VAS score  $\geq 5$  cm; Figure 2D).

## Interfaces specifications

### *Collecting information*

*Allergy Diary Companion* screen interfaces for collecting VAS score for the e-CDSS is shown in Figure 3A. The VAS question is ‘overall how much are your allergic symptoms bothering you today?’ and is identical to that used in the *Allergy Diary* for patients, ensuring that both physicians and patients are speaking the same language of AR control. This allows for inter-connectivity between applications, consistency of AR control assessment and computation. The *Allergy Diary Companion* screen Interfaces for collecting information on AR medication use, AR phenotype and allergen exposure (Module 3) are shown in S-Figure 5.

### Summarizing information

The following information is summarized by *Allergy Diary Companion* for providers (Figure 3B):

- AR disease control status message: ‘Your patient has [well-, partly- or un-] controlled allergic rhinitis.’
- Current VAS score of the patient: this is expressed as a positive integer to one decimal place. AR control is categorized according to this VAS score, and colour coded in the same way as for the *Allergy Diary* – well-controlled AR: green (VAS score <2 cm); partly controlled AR: yellow (VAS score ≥2 to <5 cm) and uncontrolled AR: orange: (VAS score ≥5 cm) (Figure 3B).
- AR phenotype: This is categorized as either ‘intermittent’ or ‘persistent’ depending on duration of treatment (or symptoms).
- Allergen exposure: summarized as either ‘yes’ or ‘no’
- Treatment: List of currently taken AR treatments.

### Treatment recommendation

A treatment recommendation is then provided based on this information, and using the rules as outlined in the e-CDSS (Figures 2A-2D) and summarized in Table 1. Treatment recommendations are in the format: Recommendation – approach – specific treatment recommendation. For the example shown in Figure 3B the recommendation is to step up treatment, as the patient has a VAS score ≥5/10 cm, has IAR (with allergen exposure) and is currently treated (with AIT and FP – i.e. T5 + T2) - see Table 1 scenario 1. The recommended treatment option is to continue the AIT course and step up symptomatic treatment to INCS + AZE (i.e. step up from T5 + T2 = T5 + T3) – see Table 1 scenario 18. By clicking on ‘INCS + AZE’ the treatment listed is ‘Dymista’, currently the only medication in this class.

## Discussion

In this article we describe a 21<sup>st</sup> century approach to AR management. m-Health refers to the use of mobile devices to collect, collate, and assess patient level health data. In this article we focus on CDSS and m-health in AR, and describe the process of transforming the recently published AR-CDSS [2] into an e-CDSS, and how this e-CDSS was embedded into an m-health tool for providers called the *Allergy Diary Companion*.

Incorporation of the e-CDSS into the *Allergy Diary Companion* was achieved in a systematic and collaborative way, by (i) generating treatment management scenarios, (ii) obtaining expert consensus on specific AR CDSS-informed treatment recommendations, allowing for variations in line with expert opinion; (iii) generating electronic algorithms to describe all scenarios within the AR CDSS; (iv) digitizing these algorithms to form the e-CDSS and finally (v) embedding the e-CDSS into the *Allergy Diary Companion* app to permit easy user interfacing. In this way the *Allergy Diary Companion* serves as a knowledge translation intervention for providers, a dynamic and iterative process that induces the synthesis, dissemination, exchange and ethically sound application of knowledge to improve health [18], encouraging change in behaviour in keeping with scientific evidence. Key experts in the field of AR from all over the world agreed on the AR CDSS approach to AR management, and on specific treatment recommendations provided by *Allergy Diary Companion* and informed by VAS score, disease phenotype, allergen exposure and treatment history. To our knowledge this is the first time the development of any m-health tool has been described in this transparent and detailed way, providing confidence, not only in the app, but also in the treatment recommendations it provides.

The *Allergy Diary Companion* is essentially a decision aid for providers. Decision aids increase knowledge, reduce decisional conflict and have a positive effect on patient-practitioner communication [19, 20], and may be particularly effective when incorporated into an e-health tool. For example, when providers use handheld computers to access clinical information, their

knowledge improves significantly more than peers who use paper resources. Physician adherence to guidelines is poor [21] and it is hoped that when guideline recommendations are presented electronically, providers may make safer prescribing decisions and adhere more closely to these recommendations vs peers using paper resources [22]. Unfortunately, at the physician level CDSSs are rarely used, and the advice is not followed [23], even though use of computerized CDSSs have been shown to improve asthma and COPD care [24]. Embedding the AR CDSS into the *Allergy Diary Companion* is expected to increase usage of the AR CDSS, resulting in improved standard of AR care in routine clinical practice, both at the physician and pharmacy levels. Indeed CDSSs have already proved beneficial at the pharmacy level [25, 26], reducing the frequency of drug-drug interactions and preventing inappropriate prescribing and under-prescribing [27]. It should also be noted that although a recently conducted Cochrane review provided no evidence that the use of electronic health information (EHI) translates into improved clinical practice or patient outcomes, it does suggest that when practitioners are provided with EHI and education or training, its use increases [28]. It was further noted that for EHI to be applied in patient care, it will be necessary to understand why practitioners' are reluctant to apply EHI when treating people, and to determine the most effective way(s) to reduce this reluctance [28].

On the patient side, mobile phone apps to improve allergy and asthma care are part of an ever-growing number of m-tools available, but their usefulness is still debated and studies have been small [29], [30]. However, a large study including 327 individuals with AR or asthma, showed that QoL was improved in AR patients and the likelihood of asthma control increased when using an app which facilitated communication with physicians and which recorded health status and medication compliance [31].

A limitation of the *Allergy Diary Companion* is that it currently relies on the input of information by patients themselves. It does not take into account data already recorded by patients in their *Allergy Diary*. In other words, there is a lack of connectivity between m-health tools. One improvement could be to upload patient data directly from the *Allergy Diary* to the *Allergy Diary Companion* (i.e. Module 5; see Figure 4). This step would need serious ethical consideration that are currently being discussed. Personal data protection is a fundamental right in Europe, enshrined in Article 8 of the Charter of Fundamental Rights of the European Union, as well as in Article 16(1) of the Treaty on the Functioning of the European Union. Guidance already exists on data protection requirements for "apps" with Opinion 2/2013 of the Article 29 Working Party of 27 February 2013 on apps on smart devices. In the EU, the currently applicable Personal Data Protection Directive is being revised in order to better respond to challenges posed by the rapid development of new technologies and globalisation while ensuring that individuals retain effective control over their personal data. The *Allergy Diary Companion* app will comply with all local and European directives. Future iterations of the *Allergy Diary Companion* may permit connectivity with pollen, air pollution, meteorologic storm warnings and google trends which may influence treatment recommendations. Finally, all *Allergy Diary Companion* app functionally and management advice needs to be validated, and this will be done prior to launch. The *Allergy Diary Companion* app is an ideal tool to assess the benefit of using the AR CDSS in a real life setting. The value of this m-health tool is that it allows for variations and modifications of the e-CDSS based on real life experience, thus moving from a consensus-based CDSS to an evidence-based one.

Other modules which may be used to 'feed' the e-CDSS could include identification of those patients at risk of allergen exposure by incorporating a pollen alert module (Module 6; Figure 4) and a sentinel network module (Module 7; Figure 4). The sentinel network is an early warning system or predictor for patients of impending symptoms. A recently obtained H2020 grant (POLLAR: Impact of air pollution in asthma and rhinitis) will help to answer this question. This system should also prove



useful in predicting asthma control deterioration in those with co-morbid rhinitis. Use of predictive algorithms have already been used in home monitoring of asthma and chronic obstructive pulmonary disease patients, but with varying degrees of success, mainly due to poor patient compliance and poor performance of conventional algorithms for detecting deteriorations [32]. These improvements to the system would essentially negate the need for Modules 1 and 3 for those users with smart phones. Modules 1 and 3 would remain in the system for those patients who do not have smartphone or do not wish to download *Allergy Diary*. Finally, a PC-based tool should also be developed, enabling physicians to import data, with individual patient consent, to their pc directly from the patient's *Allergy Diary*, interacting with *Allergy Diary Companion*, so that data may be stored as an electronic file as part of the patient's notes.

When developing any new m-health tool, the aim is to achieve a high quality and popular app, which will be used enthusiastically and provide benefit to users. This is a challenging process, and not always entirely successful, either due to design issues [33] or at the implementation stage [28, 34]. *Allergy Diary Companion* for providers has been designed to be used in conjunction with the *Allergy Diary* for patients as part of MASK (included in the B3 action plan of the European Innovation Partnership on Active and Healthy Ageing (EIA on AHA). MASK follows the JA-CHRODIS (Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle) recommendations for the evaluation of Good Practices. This means that it works well, produces good results and is recommended as a model [35]. MASK complies with equity (design and implementation), practice (e.g. appropriateness of design, SMART objectives), ethical, evaluation, empowerment/participation, target population, sustainability, governance and scalability targets [35]. Use of both apps will (i) permit patients to screen for allergic disease and monitor AR and asthma control, (ii) assist pharmacists in recommending over the counter medications and prompt referral of patients with uncontrolled AR to physicians and (iii) encourage primary care physicians to prescribe appropriate treatment, to follow-up in accordance with the AR CDSS and to refer to specialist clinics when

appropriate [36]. However, the e-CDSS does not include information on allergic multi-morbidities [37]. That will be included at a later stage.

In conclusion, the *Allergy Diary Companion* for providers has been designed to provide healthcare information to practitioners and researchers, to permit real-time monitoring of disease related data and to provide guideline and expert-endorsed AR treatment recommendations. The *Allergy Diary Companion* is currently being finalized and will be launched in 2018.

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Table 1: KOL consensus opinion and level of agreement for each scenarios of the AR CDSS

	Patient VAS	Phenotype	Tx	Consensus	Level of agreement
<b>Part 1: Approach to treatment</b>					
1	≥5	IAR or PER	Yes	Step up	91
2	≥2 to <5	IAR	Yes	Continue	76
3	<2	IAR	Yes	Step down	85
4	≥2 to <5	PER	Yes	Continue or step up	88
5	<2	PER	Yes	Step down	75
6	≥5	IAR	No	Initiate	97
7	≥5	PER	No	Initiate	98
8	<5	IAR or PER	No	Initiate	87
<b>Part 2: Specific treatment step ups</b>					
	<b>Current Tx</b>	<b>Step up</b>		<b>Notes</b>	
9	T1	T2 OR T3			91
10	T2	T3			83
11	T3	T3 + T4*		Consider T5 <sup>†</sup>	66
12	T1 + T2	T3		Consider T5 <sup>†</sup>	80
13	T1 + T3	T3 + T4*		Consider T5 <sup>†</sup>	68
14	T2 + T3	T3 + T4		Consider T5 <sup>†</sup>	66
15	T5 + VAS ≥5	T5 + T2 OR T3			80
16	T5 + VAS ≥2 to <5	T5 + T1, T2 OR T3		T5 + T2 or T3 if congestion	84
17	T5 + T1	T5 + T2 OR T3			89
18	T5 + T2	T5 + T3			86
19	T5 + T3	Continue		Consider referral	86
<b>Part 3: Specific treatment step downs</b>					
	<b>Current Tx</b>	<b>Step down</b>		<b>Notes</b>	
20	T3	T2 OR T1		T2 if congestion	78
21	T2	T1		Continue T2 if congestion	73
22	T1	Stop		NOT exposed to allergen	86
23	T1	Continue		EXPOSED to allergen	84
24	T1 + T2	T1 OR T2		T2 if congestion	87
25	T1 + T3	T1 OR T3		T3 if congestion	79
26	T2 + T3	T2 OR T3			87
27	T5 + T3	T5 + T1 OR T2		T5 + T2 if congestion	80
28	T5 + T2	T5 + T1		Continue T5 + T2 if congestion	75
29	T5 + T1	T5		NOT exposed to allergen	91
30	T5 + T1	T5 + T1		EXPOSED to allergen	83
31	T5	T5		Until end of course	97
<b>Part 4: treatment initiation</b>					
	<b>Patients</b>	<b>Tx</b>	<b>Consensus</b>	<b>Notes</b>	

<b>32</b>	IAR; VAS $\geq 5$	No	T1, T2 OR T3	T2 or T3 if congestion	83
<b>33</b>	PER; VAS $\geq 5$	No	T2 OR T3		90
<b>34</b>	IAR or PER VAS $< 5$	No	T1, T2 OR T3	T2 or T3 if congestion	87

VAS: visual analogue scale; Tx: treatment; IAR: intermittent allergic rhinitis; PER: persistent allergic rhinitis; T1: anti-histamine (oral, intranasal, eye drops), leukotriene receptor antagonist, or cromones (intranasal, eye drops); T2: intranasal corticosteroids (INCS); T3: INCS + azelastine; T4: oral corticosteroid; T5: consider referral and allergen-specific immunotherapy.

\* short course (3-7 days); †if VAS score remains  $\geq 5/10$

Level of agreement: VAS  $\geq 75$ : excellent; VAS 50-74: good



**Table 2: Modules of e-CDSS**

	Info	Description	e-CDSS decision or input	e-CDSS variable
<b>M1</b>	VAS (cm)	<2: well controlled ≥2 to <5: partly controlled ≥5: uncontrolled	<2 ≥2 to <5 ≥5	[1..5]
<b>M2</b>	Treatment classification	None AH/LTRA/cromone INCS INCS & AZE OC Consider referral & AIT	T0 T1 T2 T3 T4 T5	Ti, Tj, Tk, Tl
<b>M3</b>	Patient characteristics	<b>Q1:</b> Do you currently take AR medication?  <b>Q2a:</b> Select medication(s) <b>Q3a:</b> How many days/week do you usually take your Tx (1-7)? <b>Q4a:</b> How many consecutive weeks do you take it (1-5 or more)? <b>Q2b:</b> Is this the first time experiencing symptoms? <b>Q3b:</b> How many days/week do they last (1-7)? <b>Q4b:</b> How many consecutive weeks do they last (1-5, or more)? <b>Q5:</b> Are you currently exposed to allergen?	Current med  Scrolled list  Week ≥4 & day ≥4  First experience  Week ≥4 & day ≥4  Yes or don't know	{True/false}    {True/false} True=PER False=IAR {True/false}   {True/false} True=PER False=IAR {True/false} True=yes False=no
<b>M4</b>	CDSS	Data from M1, M2 and M3		

CDSS: clinical decision support system; VAS: visual analogue scale; AH: anti-histamine (oral, intranasal, eye drops); LTRA: leukotriene receptor antagonist; INCS: intranasal corticosteroid; AZE: azelastine; OC: oral corticosteroid; AIT: allergen-specific immunotherapy; AR: allergic rhinitis; Tx: treatment; PER: persistent AR; IAR: intermittent AR; Ti: current treatment (if multiples Ti=highest medication class); Tj,k,l: add on treatments to Ti

## Figure Legends

**Figure 1:** Steps for the development of the ARIA e-CDSS  
MACVIA: Contre les Maladies Chroniques pour un Vieillissement actif; ARIA: Allergic Rhinitis and its Impact on Asthma; AR: allergic rhinitis; CDSS: clinical decision support system; VAS: visual analogue scale; KOL: key opinion leader.

**Figure 2:** Decision processes underlying treatment recommendations for (A) patients not currently on any AR medication, (B) patients with well-controlled AR (i.e. VAS score <2), (C) patients with partly-controlled AR (i.e. VAS score  $\geq 2$  to <5) and (D) patients with uncontrolled AR (i.e. VAS score  $\geq 5$ ). AR: allergic rhinitis; VAS: visual analogue scale; M1: module 1; M2: module 2; M3: module 3; Ti: class of current treatment (in case of polypharmacy, Ti = maximum class). Tj, Tk and Tl: medications added to Ti, order of class  $k < j < i$ . T1: anti-histamine (oral, intranasal, eye drops), leukotriene receptor antagonist, cromone (intranasal, eye drops); T2: intranasal corticosteroid (INCS); T3: INCS + Azelastine; T4 add short course of oral corticosteroids; T5: consider referral and allergen-specific immunotherapy

**Figure 3:** (A) VAS scale interface of *Allergy Diary* and *Allergy Diary Companion* apps and (B) Treatment recommendation provided by e-CDSS of the *Allergy Diary Companion* app, including information from Modules 1, 2 and 3.

**Figure 4:** Schematic representation of architecture of an improved e-CDSS. M: module; Tx: treatment; e-CDSS: electronic clinical decision support system.

Figure 1

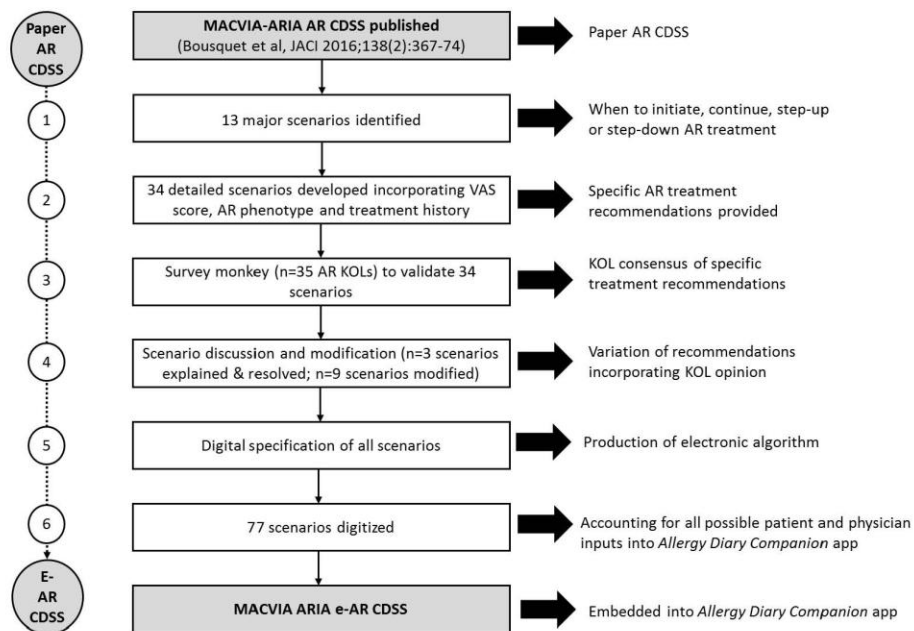


Figure 2A

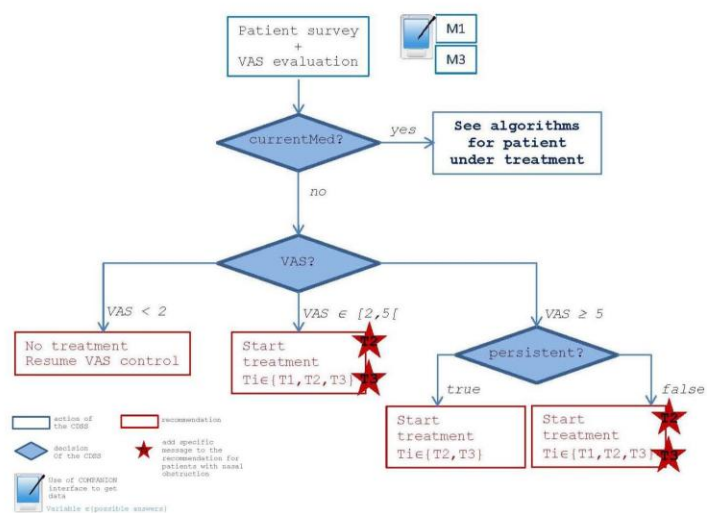


Figure 2B

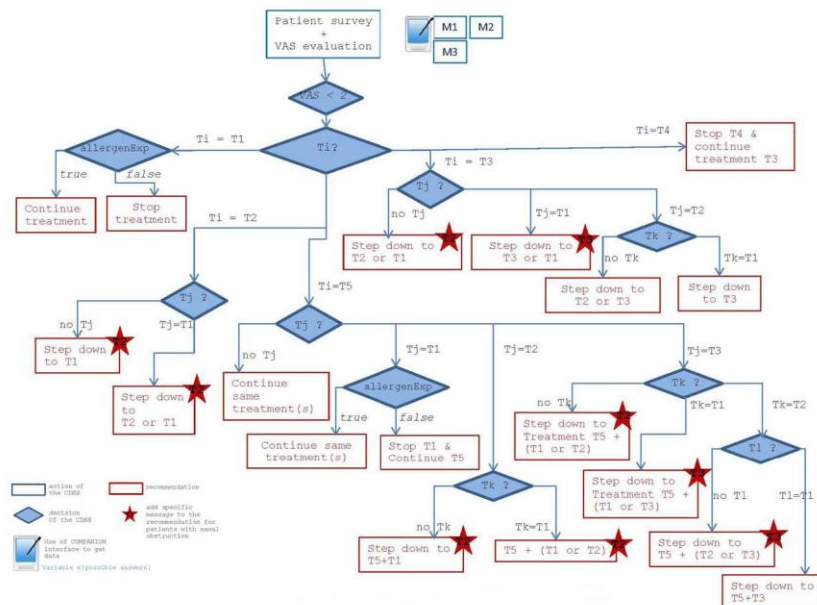


Figure 2C

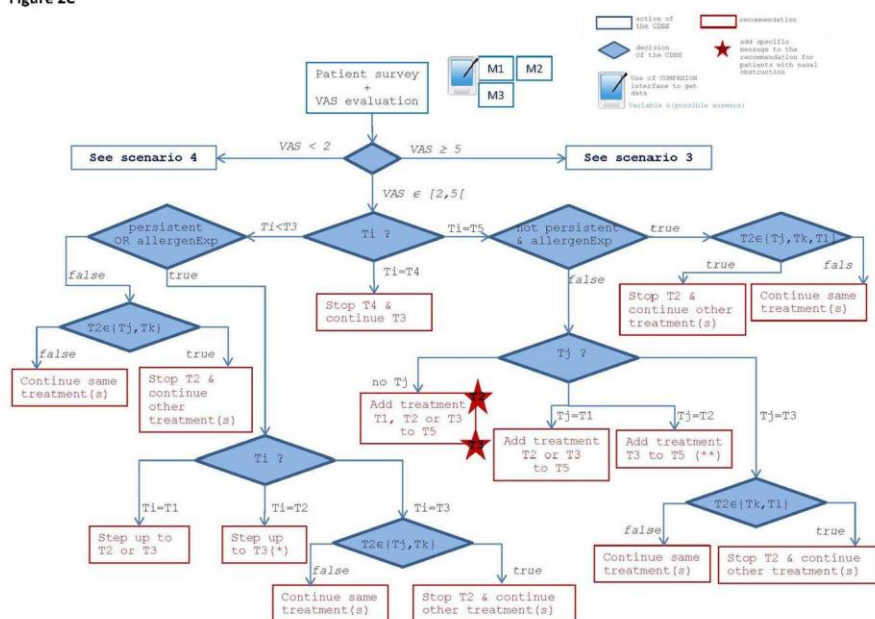


Figure 2D

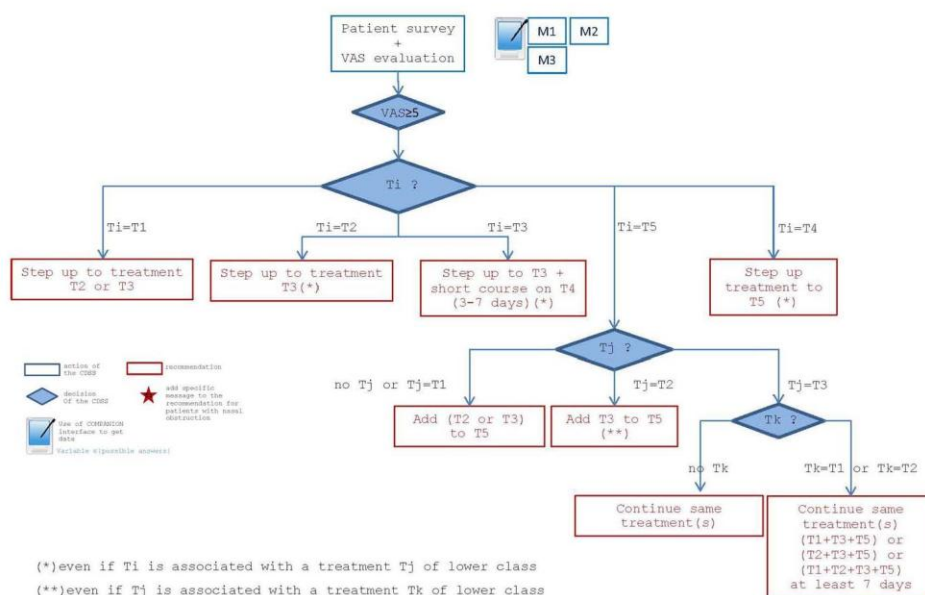


Figure 3A

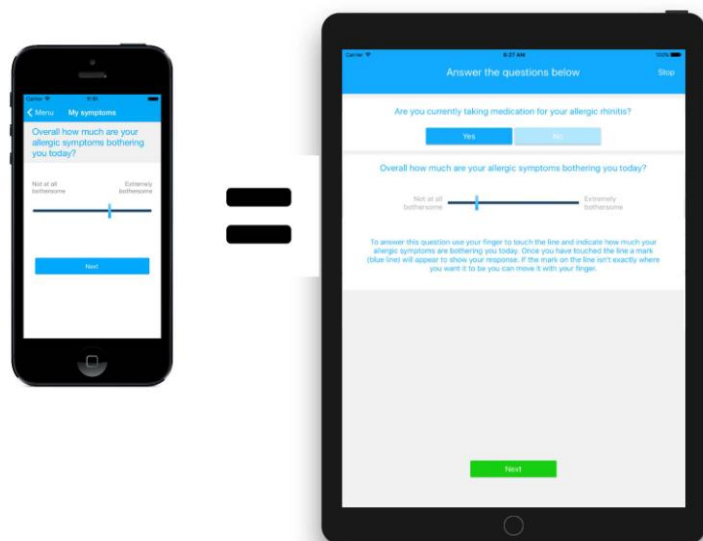




Figure 3B

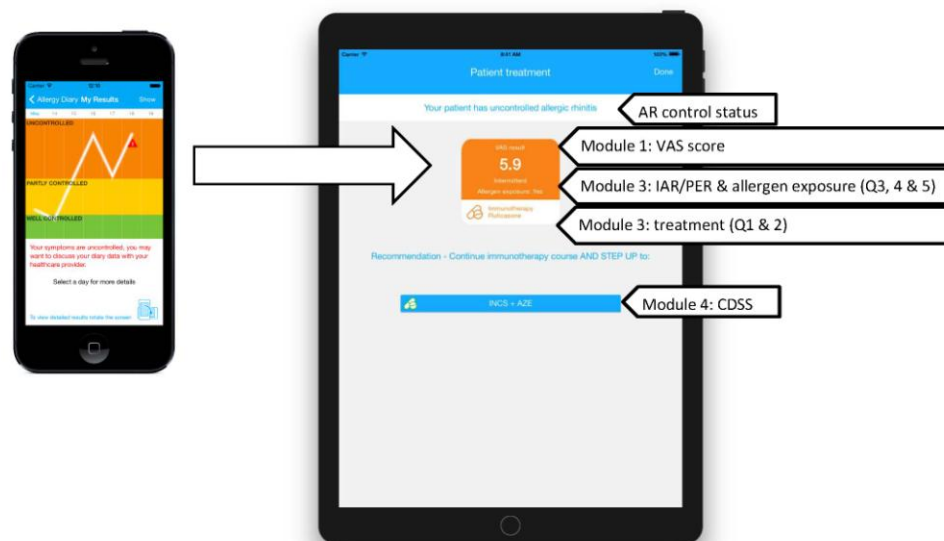


Figure 4

